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Case Report

Death from undiagnosed glioblastoma multiforme and toxic self-medication presenting with concurrent dysfunctional behavior

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Abstract

We encountered a decedent with an unexpected glioblastoma multiforme. A 61-year-old retired African–American woman was found dead in her home, fully clothed in her bathtub, with a pillow under her head. At autopsy, the brain showed a glioblastoma multiforme. Toxicology showed elevated hydrocodone, propoxyphene, acetaminophen, and positive paroxetine. The presence of a brain tumor likely caused a severe headache. The use of her medications could have indicated a reaction to the escalating pain of the brain trauma, and overuse could be consistent with escalating pain or loss of rational thought processes. The present case is interesting in that it had evidence of behavioral dysfunction that could be related to the brain tumor, and death arising from the glioblastoma multiforme (cerebral hemorrhage and edema) with concurrent multiple drug intoxication.

Keywords: Glioblastoma multiforme; Death; Autopsy; Toxicology; Overdose; Dysfunctional behavior

1. Introduction

Occult malignancies comprise a small proportion of deaths in the community, estimated at 1.7% or 2.4% in two large studies.[1,2] Within the group of deaths from occult malignancy, deaths from undiagnosed primary glioma are particularly rare.[3–5] We recently encountered a patient who was determined to have an unexpected glioblastoma multiforme at autopsy. This lesion explained several unusual circumstances of the decedent's death, and demonstrated a natural history of this malignancy when it runs its course without medical intervention.

2. Case report

The decedent was a 61-year-old retired African–American woman who lived alone. She had a history of anxiety and chronic pain for which she had prescriptions. A family member performed a well-being check when she had not responded to phone calls. She was found dead in her home, fully clothed in her bathtub, with a pillow under her head. There was no water in the tub. Bottles of medication and a cup of tea were spread along the edge of the tub. An autopsy was ordered to determine the cause and manner of death.

The body was that of a well-nourished African–American woman with no external abnormality. The chest and abdominal organs were unremarkable. She had undergone a hysterectomy in the remote past. All blood had coagulated, preventing collection of a usable specimen for drug screening. The edematous brain weighed 1320 g. There was herniation of the cerebellar tonsils. The cut surfaces of the brain showed a soft hemorrhagic area measuring 1.5 cm at junction of the midbrain and left temporal lobe.

Microscopically, the hemorrhagic area of the brain showed a glioblastoma multiforme, characterized by hypercellularity, cellular atypia, neovascularization, necrosis, and hemorrhage (Fig. 1). The adjacent brain showed edema.

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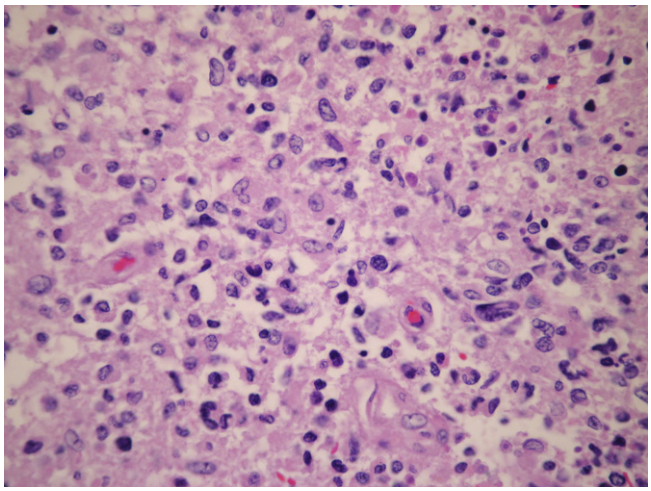

Fig. 1. Glioblastoma multiforme found at autopsy. Hypercellularity, cellular atypia, and neovascularization shown. Areas of hemorrhage and necrosis evident in elsewhere in the tumor. (Hematoxylin and eosin, 100×.)

Since blood was not available, toxicological studies were performed on vitreous humor. The studies demonstrated a hydrocodone concentration of 508 ng/mL (therapeutic 10–40 ng/mL), propoxyphene 1492 ng/mL and norpropoxyphene 615 ng/mL (therapeutic 200–800 ng/mL), acetaminophen 200 μg/mL (therapeutic 10–30 μg/mL), paroxetine 67 ng/mL (therapeutic 20–200 ng/mL). The vitreous was also positive for caffeine and nicotine.

The cause of death was assessed to be hemorrhage of a glioblastoma multiforme that caused cerebral edema and brainstem herniation, along with concurrent multiple drug intoxication.

3. Discussion

There were two potential causes of death in this decedent, a glioblastoma multiforme and intoxication with multiple drugs. We believe each contributed to her death, but the root cause of her demise was the undiagnosed glioblastoma multiforme. The presence of a brain tumor with concurrent cerebral edema and intracranial hemorrhage likely caused a severe headache as bleeding and swelling progressed. The patient may have moved to the bathroom, with proximity to the medicine cabinet and toilet, as a conscious reaction to the progressive sense of sickness and disability caused by the tumor, hemorrhage, and pain. In this sense, her behavior may have been largely rational, choosing a setting that would provide access to a toilet in case of nausea and vomiting, and access to analgesics that were kept in the medicine cabinet. Progressively using more medication may indicate the refractory nature of the pain, and the need to raise the dose and type of medication in an attempt to alleviate pain. This decision may have led to an accidental overdose. Alternatively, she may have eventually located in the bathroom as paradoxical behavior caused by the disorientation and loss of rational thought processes as the brain injury increased. The use of her medications could indicate a reaction to the escalating pain of the brain trauma, and the overuse could be consistent with loss of rational thought processes. It was interesting that she maintained comfort measures, however, such as placement of a pillow in the tub, and keeping a cup of tea handy. The fact that she remained clothed while reclining in the bathtub suggests a peculiar behavior, however, that may have been due to disorientation.

Of course, we cannot completely exclude the possibility of deliberate overdose with suicidal intent, but we consider this scenario unlikely. The coincidence that she would elect to end her life at the same time as a malignant glioma caused brain injury does not seem as plausible as the reasonable sequence of events that she responded to an intensifying headache with pain medication, and progressively lost track of her surroundings and medication use.

In large surveys of medical examiner autopsies, the numbers of malignant brain tumors that are diagnosed only at autopsy comprise a small fraction of a percent of cases[3,4]. Typically, malignant brain tumors are symptomatic early in the disease course, due to increased intracranial pressure.[3] Occasionally there is a history that the decedent of an occult brain tumor had vague neurological symptoms antemortem.[5] For such symptoms to persist at length and not be linked to a brain tumor antemortem, however, is unusual. The cause of death may be due entirely to the effect of the brain tumor.[5–7] Alternatively, the brain tumor may have led to complications that caused or facilitated death, as appears to have been the case in this decedent.[6] Rarely, the patient may have been found in acute distress antemortem and died after brief intervention, leading to the diagnosis of intracranial malignancy at autopsy.[4]

The present case is interesting in that it had both evidence of behavioral dysfunction that could be related to the brain tumor (resting in a bathtub fully clothed with tea at hand), and of imminent symptoms that could have been caused by the brain tumor (use and overuse of pain medications). While the tumor may have initiated the sequence of events that led to this setting and medication use, the role of a toxic interaction and overdose of her medications must also be considered significant factors in her death. However, it appears that the tumor and its complications, including hemorrhage and edema, initiated the chain of events that led to her drug use and death.

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